

(FILE 'HOME' ENTERED AT 10:50:23 ON 17 OCT 2005)

FILE 'REGISTRY' ENTERED AT 10:56:36 ON 17 OCT 2005

L1 242 S [HA] [AGVFS] [KCRL] R [RNSK] L [IF] F/SQSP  
L2 95 S L1 AND SQL=8  
L3 101 S [HA] [AGVF] [KRL] R [RNSK] L [IF] F/SQSP  
L4 81 S L3 AND SQL=8

FILE 'CAPLUS, USPATFULL, MEDLINE, BIOSIS' ENTERED AT 10:59:23 ON 17 OCT 2005

=> s 12

L5 12 L2

=> s 14

L6 10 L4

=> dup remo 15

PROCESSING COMPLETED FOR L5

L7 9 DUP REMO L5 (3 DUPLICATES REMOVED)

=> dup remo 16

PROCESSING COMPLETED FOR L6

L8 8 DUP REMO L6 (2 DUPLICATES REMOVED)

=> d 17 1-9 bib abs

L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

AN 2005:614582 CAPLUS

DN 143:159434

TI p21WAF1-derived peptides preferentially inhibiting cyclin E/CDK2 and  
cyclin A/CDK2 complexes for use in drug screening and therapy

IN Zheleva, Daniella I.; Fischer, Peter Martin; McInnes, Campbell; Andrews,  
Martin J. i.; Chan, Weng C.; Atkinson, Gail E.

PA Cyclacel Ltd., UK

SO U.S. Pat. Appl. Publ., 199 pp., Cont.-in-part of U.S. Ser. No. 441,952.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005153894	A1	20050714	US 2004-771242	20040413
	GB 2369823	A1	20020612	GB 2002-2889	20001129
	GB 2369823	B2	20030604		
	US 2003036628	A1	20030220	US 2000-726470	20001129
	US 2004176301	A1	20040909	US 2003-441952	20030519
	WO 2005040802	A2	20050506	WO 2004-GB4431	20041020
	WO 2005040802	A3	20050915		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,  
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,  
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,  
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,  
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,  
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
SN, TD, TG

PRAI GB 1999-28323 A 19991130  
US 2000-726470 A2 20001129  
US 2003-441952 A2 20030519  
GB 2003-24466 A 20031020  
GB 2000-29151 A3 20001129  
US 2004-771242 A 20040413

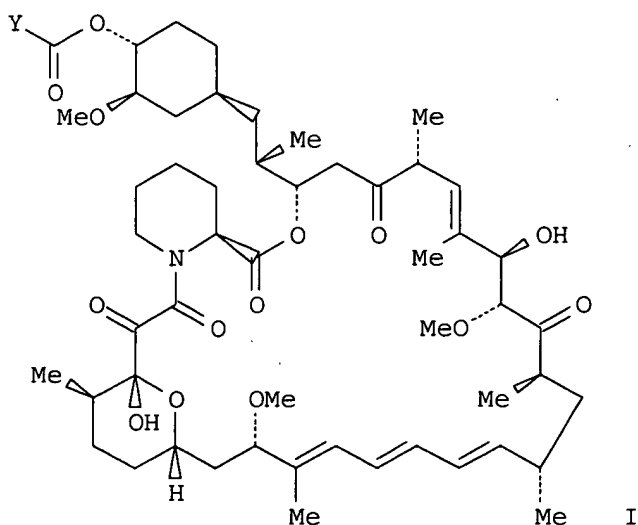
OS MARPAT 143:159434

AB Peptides derived from the cyclin dependent kinase inhibitor, p21CIP1,

including substitution analogs, that can inhibit CDK/cyclin complexes, particularly cyclins A or E with cyclin dependent kinase CDK2 are described for use in the therapeutic inhibition of the kinases in the control of cell proliferation. These peptides are derived from the sequence that binds to the cyclin-binding groove of the kinase and may be modified by the substitution of naturally-occurring amino acids with amino acid analogs. Peptides derived from a C-terminal region of p21 display selectivity for cyclin/CDK2 inhibition over cyclin/CDK4 inhibition. A variety of analogs with amino acid substitutions at different sites within the peptide were tested for their activity and selectivity of inhibition. Variants of such peptides particularly involving certain alanine replacements are shown to be particularly potent.

L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2005:409550 CAPLUS  
 DN 142:464021  
 TI Rapamycin peptides conjugates: synthesis and uses thereof  
 IN Sharma, Sanjay K.; Woo, Thomas; Naicker, Selvaraj  
 PA Altachem Pharma Ltd., Can.  
 SO PCT Int. Appl., 60 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005042567	A1	20050512	WO 2004-CA1918	20041103
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI US 2003-516273P	P	20031103		
OS MARPAT 142:464021				
GI				



AB The new rapamycin derivs. I [Y = NH-(A)n-CH2OH, NHCH(R1)(R2), NHCH(R1)(R2R3), NHC(CH2R4R7)(R5)(CH2R6R8); R10CONHCH(R1)(R2), NHR11; A = D

or L amino acid; n = 1-10; R1, R2 = H, alkyl, hydroxyalkyl, CO2R9; R3 = aryl; R4, R5, R6 = alkyl, hydroxyalkyl; R7, R8 = H, cycloalkyl, hydroxycycloalkyl; R9, R10 = alkyl; R11 = cycloalkyl; and Y linked through a carbamate ester linkage] were prepared by reacting hitrophenoxycarbonyl rapamycin and amino acid, amino alc. or peptide under basic conditions for the inhibition of cell proliferation and treating cell proliferation disorders. Thus, rapamycin derivative I (Y = O-4-C6H4-NO2) was regioselective coupled at 42 position with deprotected dipeptide H-L-Leu-D-Phe-CH2OH in piperidine to afford the conjugate rapamycin-42-O-ester I (Y = L-Leu-D-Phe-CH2OH) in 45% yield. All resulting compound were tested for cell proliferation and cell viability and showed the same or higher efficiency as rapamycin.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:395575 CAPLUS  
DN 142:435740  
TI p21WAF1-derived peptides preferentially inhibiting activity of cyclin E/CDK2 and cyclin A/CDK2 complexes for use in drug screening and therapy  
IN Zheleva, Daniella I.; Fischer, Peter M.; McInnes, Campbell; Andrews, Martin J. I.; Chan, Weng C.; Atkinson, Gail E.  
PA Cyclacel Limited, UK  
SO PCT Int. Appl., 112 pp.  
CODEN: PIXXD2

DT Patent  
LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005040802	A2	20050506	WO 2004-GB4431	20041020
	WO 2005040802	A3	20050915		
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	RW:				
	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2005153894	A1	20050714	US 2004-771242	20040413
PRAI	GB 2003-24466	A	20031020		
	US 2004-771242	A	20040413		
	GB 1999-28323	A	19991130		
	US 2000-726470	A2	20001129		
	US 2003-441952	A2	20030519		

OS MARPAT 142:435740

AB The present invention relates to p21WAF1-derived peptides capable of inhibiting CDK/cyclin complexes, particularly cyclins A or E/CDK2, by modifying the interaction with their substrates. The peptides are derived from a C-terminal region of p21 and display selectivity for cyclin/CDK2 inhibition over cyclin/CDK4 inhibition. Variants of such peptides particularly involving certain alanine replacements are shown to be particularly potent.

L7 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2  
AN 2004:739952 CAPLUS  
DN 141:256525  
TI Cyclin-binding p21WAF1 peptides and their use in drug screening assays to identify inhibitors of cyclin-dependent kinases  
IN Zheleva, Daniella I.; Fischer, Peter M.; McInnes, Campbell; Andrews, Martin J. I.; Chan, Weng C.; Atkinson, Gail E.  
PA Cyclacel Limited, UK  
SO U.S. Pat. Appl. Publ., 193 pp., Cont.-in-part of U.S. Ser. No. 726,470.  
CODEN: USXXCO

DT Patent  
LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004176301	A1	20040909	US 2003-441952	20030519
	GB 2369823	A1	20020612	GB 2002-2889	20001129
	GB 2369823	B2	20030604		
	US 2003036628	A1	20030220	US 2000-726470	20001129
	US 2005153894	A1	20050714	US 2004-771242	20040413
PRAI	GB 1999-28323	A	19991130		
	US 2000-726470	A2	20001129		
	GB 2000-29151	A3	20001129		
	US 2003-441952	A2	20030519		
	GB 2003-24466	A	20031020		

AB The present invention relates to p21WAF1-derived peptides capable of inhibiting CDK/cyclin complexes, particularly cyclin A/CKD2 or cyclin E/CDK2, by modifying the interaction with their substrates. The peptides are derived from a C-terminal region of p21WAF1 and selectively inhibit cyclin/CDK2 over cyclin/CDK4. Variants of such peptides particularly involving certain alanine replacements are shown to be particularly potent.

L7 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3

AN 2004:155698 CAPLUS

DN 140:193041

TI Polyadenylate polymerase cyclin recognition motif peptide that kills growing but not stationary cells, and therapeutic use

IN Bond, Gareth Lane; Manley, James L.; Prives, Carol

PA The Trustees of Columbia University In the City of New York, USA

SO U.S., 27 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6696546	B1	20040224	US 2000-707263	20001106
PRAI	US 2000-707263		20001106		

AB The invention provides purified and synthetic peptides, as well as pharmaceutical compns. comprising the peptides and methods of killing dividing cells and treating abnormalities and tumors in a subject using the peptides. The peptides of the invention include a polyadenylate polymerase cyclin recognition motif (PAP CRM), as well as a membrane-permeable version of PAP CRM.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 9 USPATFULL on STN

AN 2003:51670 USPATFULL

TI p21 peptides

IN Zheleva, Daniella I., Newport on Tay, UNITED KINGDOM

Fischer, Peter M., Arbroath, UNITED KINGDOM

McInnes, Campbell, Longforgan, UNITED KINGDOM

Andrews, Martin J.I., Dundee, UNITED KINGDOM

Chan, Weng C., Nottingham, UNITED KINGDOM

Atkinson, Gail E., Beverley, UNITED KINGDOM

PI US 2003036628 A1 20030220

AI US 2000-726470 A1 20001129 (9)

PRAI GB 1999-28323 19991130

DT Utility

FS APPLICATION

LREP LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109

CLMN Number of Claims: 54

ECL Exemplary Claim: 1

DRWN 6 Drawing Page(s)

LN.CNT 4274

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to p21 derived peptides capable of inhibiting CDK/cyclin complexes, particularly cyclins A or E/CDK2, by modifying the interaction with their substrates. The peptides are derived from a C-terminal region of p21 and display selectivity for cyclin/CDK2 inhibition over cyclin/CDK4 inhibition. Variants of such peptides particularly involving certain alanine replacements are shown to be particularly potent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:641092 CAPLUS

DN 138:106980

TI Peptide inhibitors of CDK2-cyclin A that target the cyclin recruitment-site: structural variants of the C-Terminal Phe

AU Atkinson, Gail E.; Cowan, Angela; McInnes, Campbell; Zheleva, Daniella I.; Fischer, Peter M.; Chan, Weng C.

CS School of Pharmaceutical Sciences, University of Nottingham, Nottingham, NG7 2RD, UK

SO Bioorganic & Medicinal Chemistry Letters (2002), 12(18), 2501-2505  
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Science Ltd.

DT Journal

LA English

OS CASREACT 138:106980

AB A focused series of octapeptides based on the lead compound H-His-Ala-Lys-Arg-Arg-Leu-Ile-Phe-NH<sub>2</sub> (1), in which the C-terminal phenylalanine residue was replaced by  $\alpha$  and/or  $\beta$ -modified variants, was synthesized using solid-phase chemical Both the L-threo- $\beta$ -hydroxy-phenylalanine ( $\beta$ -phenylserine, Pse) and (2S)-phenylalaninol derivs., as competitive binders at the cyclin-recruitment site, displayed potent inhibitory activity towards the CDK2-cyclin A complex. Unexpectedly, the D-threo-Pse derivs. also showed inhibitory activity.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:858994 CAPLUS

DN 138:182972

TI Highly potent p21WAF1-derived peptide inhibitors of CDK-mediated pRb phosphorylation: delineation and structural insight into their interactions with cyclin A

AU Zheleva, D. I.; McInnes, C.; Gavine, A.-L.; Zhelev, N. Z.; Fischer, P. M.; Lane, D. P.

CS Cyclacel Ltd, Dundee, DD1 5JJ, UK

SO Journal of Peptide Research (2002), 60(5), 257-270  
CODEN: JPERFA; ISSN: 1397-002X

PB Blackwell Munksgaard

DT Journal

LA English

AB The tumor suppressor protein p21WAF1 plays a central role in regulating eukaryotic cell-cycle progression. Through its association with G1- and S-phase CDK complexes it regulates activation of the retinoblastoma protein (pRb) and E2F transcription factors. Recognition of CDK/cyclin complexes by p21 occurs, at least in part, through a protein-protein interaction with a binding groove on the cyclin subunit. The same groove has been shown to be involved in the recruitment of macromol. CDK substrates, including pRb and E2F. Blocking of this recruitment site therefore prevents recognition and subsequent phosphorylation of CDK substrates and offers a therapeutic approach towards restoration of p21-like tumor suppression. Starting from the C-terminal cyclin-binding domain of p21 we have identified the minimal and optimized bioactive 152HAKRRLLIF159 peptide sequence with respect to CDK protein kinase inhibition where pRb is the substrate. The phosphorylation of histone H1, however, which does not contain a recognizable cyclin-binding motif, was unaffected. Detailed structure-activity relationship investigations revealed that the determinants within this sequence are residues Arg155,

Leu157 and Phe159 and more completely define the composition of the cyclin-binding motif. A marked increase in potency was obtained upon replacement of the native Ser153 with an Ala residue in the context of short synthetic peptide inhibitors and significantly, this mutation resulted in comparable affinity with CDK2/cyclin A as does the full-length recombinant p21 (which has CDK2 and cyclin A binding sites). Peptides derived from various proteins known to interact with cyclins were compared for potency and selectivity. A mol. model of the complex between the cyclin groove and the HAKRRLLIF peptide was constructed. This model accounts for the observed peptide structure-activity relationships, including the potency enhancement of the LIF sequence occupying the hydrophobic pocket. Furthermore, it provides generic insights into mol. interactions governing cyclin groove recognition and lays the foundation for the development of peptidomimetic inhibitors of CDKs.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:416863 CAPLUS  
DN 135:14300  
TI Cyclin-inhibiting p21 peptides  
IN Zheleva, Daniella I.; Fischer, Peter M.; Mcinnes, Campbell; Andrews, Martin J. I.; Chan, Weng C.; Atkinson, Gail E.  
PA Cyclacel Limited, UK  
SO PCT Int. Appl., 102 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001040142	A2	20010607	WO 2000-GB4550	20001129
	WO 2001040142	A3	20020510		
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 2001017171	A5	20010612	AU 2001-17171	20001129
	GB 2358864	A1	20010808	GB 2000-29151	20001129
	GB 2358864	B2	20021113		
	GB 2369823	A1	20020612	GB 2002-2889	20001129
	GB 2369823	B2	20030604		
	EP 1250353	A2	20021023	EP 2000-979782	20001129
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRAI	GB 1999-28323	A	19991130		
	GB 2000-29151	A3	20001129		
	WO 2000-GB4550	W	20001129		

OS MARPAT 135:14300

AB The present invention relates to p21 derived peptides capable of inhibiting CDK/cyclin complexes, particularly cyclins A or E/CDK2, by modifying the interaction with their substrates. The peptides are derived from a C-terminal region of p21 and display selectivity for cyclin/CDK2 inhibition over cyclin/CDK4 inhibition. Variants of such peptides particularly involving certain alanine replacements are shown to be particularly potent.

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 L2 95 S L1 AND SQL=8  
 L3 101 S [HA] [AGVF] [KRL] R [RNSK] L [IF] F/SQSP  
 L4 81 S L3 AND SQL=8

FILE 'CAPLUS, USPATFULL, MEDLINE, BIOSIS' ENTERED AT 10:59:23 ON 17 OCT 2005

L5 12 S L2  
 L6 10 S L4  
 L7 9 DUP REMO L5 (3 DUPLICATES REMOVED)  
 L8 8 DUP REMO L6 (2 DUPLICATES REMOVED)

=> d 18 1-8 bib abs

L8 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1  
 AN 2005:614582 CAPLUS  
 DN 143:159434  
 TI p21WAF1-derived peptides preferentially inhibiting cyclin E/CDK2 and cyclin A/CDK2 complexes for use in drug screening and therapy  
 IN Zheleva, Daniella I.; Fischer, Peter Martin; Mcinnes, Campbell; Andrews, Martin J. i.; Chan, Weng C.; Atkinson, Gail E.  
 PA Cyclacel Ltd., UK  
 SO U.S. Pat. Appl. Publ., 199 pp., Cont.-in-part of U.S. Ser. No. 441,952.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005153894	A1	20050714	US 2004-771242	20040413
	GB 2369823	A1	20020612	GB 2002-2889	20001129
	GB 2369823	B2	20030604		
	US 2003036628	A1	20030220	US 2000-726470	20001129
	US 2004176301	A1	20040909	US 2003-441952	20030519
	WO 2005040802	A2	20050506	WO 2004-GB4431	20041020
	WO 2005040802	A3	20050915		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
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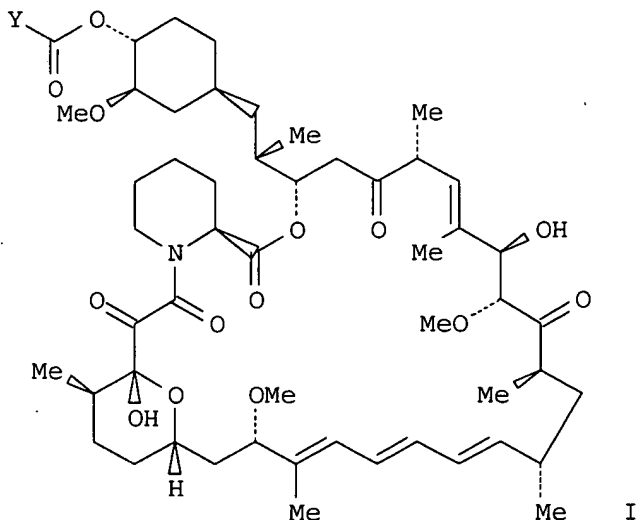
PRAI	GB 1999-28323	A	19991130
	US 2000-726470	A2	20001129
	US 2003-441952	A2	20030519
	GB 2003-24466	A	20031020
	GB 2000-29151	A3	20001129
	US 2004-771242	A	20040413

OS MARPAT 143:159434

AB Peptides derived from the cyclin dependent kinase inhibitor, p21CIP1, including substitution analogs, that can inhibit CDK/cyclin complexes, particularly cyclins A or E with cyclin dependent kinase CDK2 are described for use in the therapeutic inhibition of the kinases in the control of cell proliferation. These peptides are derived from the sequence that binds to the cyclin-binding groove of the kinase and may be modified by the substitution of naturally-occurring amino acids with amino acid analogs. Peptides derived from a C-terminal region of p21 display selectivity for cyclin/CDK2 inhibition over cyclin/CDK4 inhibition. A variety of analogs with amino acid substitutions at different sites within the peptide were tested for their activity and selectivity of inhibition. Variants of such peptides particularly involving certain alanine replacements are shown to be particularly potent.

L8 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2005:409550 CAPLUS  
 DN 142:464021  
 TI Rapamycin peptides conjugates: synthesis and uses thereof  
 IN Sharma, Sanjay K.; Woo, Thomas; Naicker, Selvaraj  
 PA Altachem Pharma Ltd., Can.  
 SO PCT Int. Appl., 60 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005042567	A1	20050512	WO 2004-CA1918	20041103
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
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PRAI	US 2003-516273P	P	20031103		
OS	MARPAT 142:464021				
GI					



AB The new rapamycin derivs. I [Y = NH-(A)<sub>n</sub>-CH<sub>2</sub>OH, NHCH(R<sub>1</sub>)(R<sub>2</sub>), NHCH(R<sub>1</sub>)(R<sub>2</sub>R<sub>3</sub>), NHC(CH<sub>2</sub>R<sub>4</sub>R<sub>7</sub>)(R<sub>5</sub>)(CH<sub>2</sub>R<sub>6</sub>R<sub>8</sub>); R<sub>10</sub>CONHCH(R<sub>1</sub>)(R<sub>2</sub>), NHR<sub>11</sub>; A = D or L amino acid; n = 1-10; R<sub>1</sub>, R<sub>2</sub> = H, alkyl, hydroxyalkyl, CO<sub>2</sub>R<sub>9</sub>; R<sub>3</sub> = aryl; R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub> = alkyl, hydroxyalkyl; R<sub>7</sub>, R<sub>8</sub> = H, cycloalkyl, hydroxycycloalkyl; R<sub>9</sub>, R<sub>10</sub> = alkyl; R<sub>11</sub> = cycloalkyl; and Y linked through a carbamate ester linkage] were prepared by reacting hitrophenoxycarbonyl rapamycin and amino acid, amino alc. or peptide under basic conditions for the inhibition of cell proliferation and treating cell proliferation disorders. Thus, rapamycin derivative I (Y = O-4-C<sub>6</sub>H<sub>4</sub>-NO<sub>2</sub>) was regioselective coupled at 42 position with deprotected dipeptide H-L-Leu-D-Phe-CH<sub>2</sub>OH in piperidine to afford the conjugate rapamycin-42-O-ester I (Y = L-Leu-D-Phe-CH<sub>2</sub>OH) in 45% yield. All resulting compound were tested for cell proliferation and cell viability and showed the same or higher efficiency as rapamycin.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD



## ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2005:395575 CAPLUS  
 DN 142:435740  
 TI p21WAF1-derived peptides preferentially inhibiting activity of cyclin  
 E/CDK2 and cyclin A/CDK2 complexes for use in drug screening and therapy  
 IN Zheleva, Daniella I.; Fischer, Peter M.; McInnes, Campbell; Andrews,  
 Martin J. I.; Chan, Weng C.; Atkinson, Gail E.  
 PA Cyclacel Limited, UK  
 SO PCT Int. Appl., 112 pp.  
 CODEN: PIXXD2

DT Patent  
 LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005040802	A2	20050506	WO 2004-GB4431	20041020
	WO 2005040802	A3	20050915		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				
	CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				
	GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				
	LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				
	NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				
	TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW:				
	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,				
	AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,				
	EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,				
	SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,				
	SN, TD, TG				
	US 2005153894	A1	20050714	US 2004-771242	20040413
PRAI	GB 2003-24466	A	20031020		
	US 2004-771242	A	20040413		
	GB 1999-28323	A	19991130		
	US 2000-726470	A2	20001129		
	US 2003-441952	A2	20030519		
OS	MARPAT 142:435740				

AB The present invention relates to p21WAF1-derived peptides capable of  
 inhibiting CDK/cyclin complexes, particularly cyclins A or E/CDK2, by  
 modifying the interaction with their substrates. The peptides are derived  
 from a C-terminal region of p21 and display selectivity for cyclin/CDK2  
 inhibition over cyclin/CDK4 inhibition. Variants of such peptides  
 particularly involving certain alanine replacements are shown to be  
 particularly potent.

L8 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2  
 AN 2004:739952 CAPLUS  
 DN 141:256525  
 TI Cyclin-binding p21WAF1 peptides and their use in drug screening assays to  
 identify inhibitors of cyclin-dependent kinases  
 IN Zheleva, Daniella I.; Fischer, Peter M.; McInnes, Campbell; Andrews,  
 Martin J. I.; Chan, Weng C.; Atkinson, Gail E.  
 PA Cyclacel Limited, UK  
 SO U.S. Pat. Appl. Publ., 193 pp., Cont.-in-part of U.S. Ser. No. 726,470.  
 CODEN: USXXCO

DT Patent  
 LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004176301	A1	20040909	US 2003-441952	20030519
	GB 2369823	A1	20020612	GB 2002-2889	20001129
	GB 2369823	B2	20030604		
	US 2003036628	A1	20030220	US 2000-726470	20001129
	US 2005153894	A1	20050714	US 2004-771242	20040413
PRAI	GB 1999-28323	A	19991130		
	US 2000-726470	A2	20001129		
	GB 2000-29151	A3	20001129		

US 2003-441952 A2 20030519  
GB 2003-24466 A 20031020

AB The present invention relates to p21WAF1-derived peptides capable of inhibiting CDK/cyclin complexes, particularly cyclin A/CDK2 or cyclin E/CDK2, by modifying the interaction with their substrates. The peptides are derived from a C-terminal region of p21WAF1 and selectively inhibit cyclin/CDK2 over cyclin/CDK4. Variants of such peptides particularly involving certain alanine replacements are shown to be particularly potent.

L8 ANSWER 5 OF 8 USPATFULL on STN  
AN 2003:51670 USPATFULL  
TI p21 peptides  
IN Zheleva, Daniella I., Newport on Tay, UNITED KINGDOM  
Fischer, Peter M., Arbroath, UNITED KINGDOM  
McInnes, Campbell, Longforgan, UNITED KINGDOM  
Andrews, Martin J.I., Dundee, UNITED KINGDOM  
Chan, Weng C., Nottingham, UNITED KINGDOM  
Atkinson, Gail E., Beverley, UNITED KINGDOM  
PI US 2003036628 A1 20030220  
AI US 2000-726470 A1 20001129 (9)  
PRAI GB 1999-28323 19991130  
DT Utility  
FS APPLICATION  
LREP LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109  
CLMN Number of Claims: 54  
ECL Exemplary Claim: 1  
DRWN 6 Drawing Page(s)  
LN.CNT 4274

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to p21 derived peptides capable of inhibiting CDK/cyclin complexes, particularly cyclins A or E/CDK2, by modifying the interaction with their substrates. The peptides are derived from a C-terminal region of p21 and display selectivity for cyclin/CDK2 inhibition over cyclin/CDK4 inhibition. Variants of such peptides particularly involving certain alanine replacements are shown to be particularly potent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2002:641092 CAPLUS  
DN 138:106980  
TI Peptide inhibitors of CDK2-cyclin A that target the cyclin recruitment-site: structural variants of the C-Terminal Phe  
AU Atkinson, Gail E.; Cowan, Angela; McInnes, Campbell; Zheleva, Daniella I.; Fischer, Peter M.; Chan, Weng C.  
CS School of Pharmaceutical Sciences, University of Nottingham, Nottingham, NG7 2RD, UK  
SO Bioorganic & Medicinal Chemistry Letters (2002), 12(18), 2501-2505  
CODEN: BMCLE8; ISSN: 0960-894X  
PB Elsevier Science Ltd.  
DT Journal  
LA English  
OS CASREACT 138:106980  
AB A focused series of octapeptides based on the lead compound H-His-Ala-Lys-Arg-Arg-Leu-Ile-Phe-NH<sub>2</sub> (1), in which the C-terminal phenylalanine residue was replaced by  $\alpha$  and/or  $\beta$ -modified variants, was synthesized using solid-phase chemical. Both the L-threo- $\beta$ -hydroxy-phenylalanine ( $\beta$ -phenylserine, Pse) and (2S)-phenylalaninol derivs., as competitive binders at the cyclin-recruitment site, displayed potent inhibitory activity towards the CDK2-cyclin A complex. Unexpectedly, the D-threo-Pse derivs. also showed inhibitory activity.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:858994 CAPLUS  
 DN 138:182972  
 TI Highly potent p21WAF1-derived peptide inhibitors of CDK-mediated pRb phosphorylation: delineation and structural insight into their interactions with cyclin A  
 AU Zheleva, D. I.; McInnes, C.; Gavine, A.-L.; Zhelev, N. Z.; Fischer, P. M.; Lane, D. P.  
 CS Cyclacel Ltd, Dundee, DD1 5JJ, UK  
 SO Journal of Peptide Research (2002), 60(5), 257-270  
 CODEN: JPERFA; ISSN: 1397-002X  
 PB Blackwell Munksgaard  
 DT Journal  
 LA English  
 AB The tumor suppressor protein p21WAF1 plays a central role in regulating eukaryotic cell-cycle progression. Through its association with G1- and S-phase CDK complexes it regulates activation of the retinoblastoma protein (pRb) and E2F transcription factors. Recognition of CDK/cyclin complexes by p21 occurs, at least in part, through a protein-protein interaction with a binding groove on the cyclin subunit. The same groove has been shown to be involved in the recruitment of macromol. CDK substrates, including pRb and E2F. Blocking of this recruitment site therefore prevents recognition and subsequent phosphorylation of CDK substrates and offers a therapeutic approach towards restoration of p21-like tumor suppression. Starting from the C-terminal cyclin-binding domain of p21 we have identified the minimal and optimized bioactive 152HAKRRLIF159 peptide sequence with respect to CDK protein kinase inhibition where pRb is the substrate. The phosphorylation of histone H1, however, which does not contain a recognizable cyclin-binding motif, was unaffected. Detailed structure-activity relationship investigations revealed that the determinants within this sequence are residues Arg155, Leu157 and Phe159 and more completely define the composition of the cyclin-binding motif. A marked increase in potency was obtained upon replacement of the native Ser153 with an Ala residue in the context of short synthetic peptide inhibitors and significantly, this mutation resulted in comparable affinity with CDK2/cyclin A as does the full-length recombinant p21 (which has CDK2 and cyclin A binding sites). Peptides derived from various proteins known to interact with cyclins were compared for potency and selectivity. A mol. model of the complex between the cyclin groove and the HAKRRLIF peptide was constructed. This model accounts for the observed peptide structure-activity relationships, including the potency enhancement of the LIF sequence occupying the hydrophobic pocket. Furthermore, it provides generic insights into mol. interactions governing cyclin groove recognition and lays the foundation for the development of peptidomimetic inhibitors of CDKs.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2001:416863 CAPLUS  
 DN 135:14300  
 TI Cyclin-inhibiting p21 peptides  
 IN Zheleva, Daniella I.; Fischer, Peter M.; McInnes, Campbell; Andrews, Martin J. I.; Chan, Weng C.; Atkinson, Gail E.  
 PA Cyclacel Limited, UK  
 SO PCT Int. Appl., 102 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001040142	A2	20010607	WO 2000-GB4550	20001129
	WO 2001040142	A3	20020510		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,			

YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001017171	A5	20010612	AU 2001-17171	20001129
GB 2358864	A1	20010808	GB 2000-29151	20001129
GB 2358864	B2	20021113		
GB 2369823	A1	20020612	GB 2002-2889	20001129
GB 2369823	B2	20030604		
EP 1250353	A2	20021023	EP 2000-979782	20001129

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI GB 1999-28323	A	19991130
GB 2000-29151	A3	20001129
WO 2000-GB4550	W	20001129

OS MARPAT 135:14300

AB The present invention relates to p21 derived peptides capable of inhibiting CDK/cyclin complexes, particularly cyclins A or E/CDK2, by modifying the interaction with their substrates. The peptides are derived from a C-terminal region of p21 and display selectivity for cyclin/CDK2 inhibition over cyclin/CDK4 inhibition. Variants of such peptides particularly involving certain alanine replacements are shown to be particularly potent.

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